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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,547	11/16/2005	Chaitan Khosla	STAN-258US5	3888

77974 7590 11/19/2009

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
11/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,547	KHOSLA ET AL.	
	Examiner	Art Unit	
	JACOB CHEU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,29-34,36 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,29-34,36 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's amendment and R1.31, 1.32 affidavits filed on 7/14/2009 has been received and entered into record and considered.
The following information provided in the amendment affects the instant application:

Claims 1-22, 25-28. 35 and 37 have been cancelled.
Claims 23-24, 29-34, 36 and 38 are pending and under examination.

2. The rejection on the new matter of claims 36-37 are withdrawn.
The rejections on Claims 23-24 under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (WO 03104273) in view of Campbell (section 1.3.4. page 29; Monoclonal Antibody Technology (1984) Elsevier Science Publishers) are withdrawn due to the evidence of priority provided by Applicants.

3. The rejections on Claims 23-24, 29-35, 38 under 35 U.S.C. 103(a) as being unpatentable over Hausch et al. (US 7303871) in view of Campbell are withdrawn because of affidavits indicating Applicants are the sole inventors in the recited subject matters.

4. The rejections of claims 23-24 under 35 U.S.C. 103(a) as being unpatentable over Arentz-Hansen et al. in view of Campbell ***are maintained***.

5. **A new ground of rejection** is also set forth in this current Office Action in view of the Arentz-Hansen and Campbell et al. prior arts.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 23-24, 29-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arentz-Hansen et al. in view of Campbell.

First, for claims 23-24, the rejections are ***maintained*** (see below; also includes claim 32).

Arentz-Hansen et al. study Celiac Sprue disease. Arentz-Hansen et al. study several alpha-gliadins for the CD412/CD387 recognition. Arentz-Hansen et al. found out one particular peptide, alpha 2 (62-75) PQPQLPYPQPQLPY, has particular function to stimulate T cell recognition (See Table II; page 606). Such 14-mer peptide is encompassed **within** SEQ ID NO. 12 (emphasis added).

). Although Arentz-Hansen et al. do not explicitly teach producing antibody (using hybridom cell line) against this polypeptide, it would have been obvious to one ordinary skill in the art to make antibodies once the antigen has been isolated. Such recognition has been endorsed by this Office. For example, *Board of Patent Appeals and interferences* has taken the position that once an antigen has been isolated and sequenced, the manufacture of monoclonal antibodies against it is *prima facie* obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. APp. & Int. 1990). Furthermore, Campbell teaches that *"it*

is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it- sometimes without a clear objective for their application." (See ch. 1, section 1.3.4. page 29).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the conventional method of producing antibody as suggested by Campbell once the peptide of interest is available as taught by Arentz-Hansen et al. since it is considered a routine "customary practice" in the art to make specific monoclonal antibody recognizing the particular peptides. Note, the sequence taught by Arentz-Hansen et al. having 14 amino acid residues which is within the 33 amino acid residues of SEQ ID No. 12. As well-known in the field, antibody usually recognizes 6-8 amino acids as binding epitopes. Without disclosing particular binding region on the SEQ ID No. 12 in the current application, the antibody produced by the Arentz-Hansen et al. and Campbell would be able to bind to the SEQ ID No. 12.

With respect to claims 29-30, and 36, 38, the recited claims fall into category of product by process claim format. The process feature includes antibody "generated against SEQ ID No. 12" (claim 29), or "generated by a response to a purified oligopeptide having the amino acid sequnce SEQ ID No. 12" (claim 30), or "produced by a cell line generated by a response to a tissue transglutaminase linked to SEQ ID No. 12" (claim 36), or generated by an immune response to a tissue glutaminase and linked to SEQ ID NO. 12"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)". Herein the claimed product is an antibody or antibody producing cell line which can bind to SEQ ID No. 12. The combined prior art mentioned above can produce an antibody/or monclonal antibody cell line functions the same, i.e. bind to SEQ ID No. 12.

9. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hruska et al. (US 6294320) in view of Campbell.

Hruska et al. teach a rabbit antibody directed against tissue transglutaminase. However, Hruska et al. do not teach producing a cell line for the above antibody. As established earlier in this Office Action, Campbell teaches routine techniques for generating cell line of monoclonal antibodies. Thus, it would have been prima facie to one ordinary skill in the art at the time the invention was made to have motivated Hruska et al. to use technique taught by Campbell to produce antibody cell line against tissue transglutaminase.

Response to Applicant's Arguments

10. Quotes from Remarks: "Applicants respectfully submit that Arentz-Hansen et al. does not teach or suggest the
presently claimed invention. Applicants' claims are directed to an antibody that specifically binds to a purified oligopeptide having the amino acid sequence LQLQPFPQPQLPYPQPQLPYPQPQLPYPQPQPF (SEQ ID NO:12).

While the peptides disclosed by Arentz-Hansen have similarities to those set forth by Applicants, the actual antigenic peptide in the publication differs from that of the present claims. The term "epitope" as used by Arentz-Hansen refers to an epitope that is recognized by a T cell. While there can be considerable overlap between epitopes recognized by antibodies and epitopes recognized by T cells, there are also significant differences. Many of these differences are a reflection of the requirement that a peptide be "presented" by an HLA antigen in order to be recognized by a T cell.

As stated in the abstract of the reference:

The great majority of patients that are intolerant of wheat gluten protein due to celiac disease (CD) are human histocompatibility leukocyte antigen (HLA)-DQ2^{+}, and the remaining few normally express HLA-DQ8. These two class II molecules are chiefly responsible for the presentation of gluten peptides to the gluten-specific T cells that are found only in the gut of CD patients but not of controls. Interestingly, tissue transglutaminase (tTG)-mediated deamidation of gliadin plays an important role in recognition of this food antigen by intestinal T cells. Here we have used recombinant antigens to demonstrate that the intestinal T cell response to ~-gliadin in adult CD is

focused on two immunodominant, DQ2-restricted peptides that overlap by a seven-residue fragment of gliadin. We show that tTG converts a ,qlutamine residue within this fraqment into glutamic acid and that this process is criticat for T cell recoqnition. (underlining added). Thus, it is not the native peptide, which sequence is a subset of SEQ ID NO:12, that is an epitope in the prior art, but a deamidated version of the peptide. As shown in Figure 2 of Arentz-Hansen, it is onry after deamidation that the peptides act as epitopes for the T cell. Applicants respectfully submit that Arentz-Hansen teaches away from the present invention, and teaches that only a deamidated derivative of the peptide disclosed therein would be an effective epitopefor T cell immune recognition of the peptide disclosed therein. While reserving the right to pursue claims of the original scope in a later filing, in order to expedite prosecution Applicants have canceled the claims or portions of claims herein that reference such deamidated epitopes.

Applicant's arguments have been considered but are persuasive.

Examiner acknowledges the data from Arentz-Hansen et al. experiments, particularly Figure 2 (B). There are three peptides used in this experiment, namely wild type (untreated), treated with tTG or treated with acid/heat. The results show that the treated ones demonstrating better recognition (binding).

In view of Campbell teachings on making polyclonal and monoclonal antibody, "*"it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it- sometimes without a clear objective for their application."* (See ch. 1, section 1.3.4. page 29)". One ordinary skill in the art would have made antibodies against all three peptides in a customary way even "without a clear objective of their application". Nevertheless, at least one artisan can make the wild type peptide serving as a control.

Furthermore, it is noted that the instant antibody can also bind to deaminated counterpart (although Applicant has deleted such feature from claim 32). Therefore, one can use the tTG treated deaminated peptide as immungen to generate antibody capable of binding to deaminated peptide which also can bind to SEQ ID No. 12.

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JACOB CHEU whose telephone number is (571)272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jacob Cheu/
Primary Examiner, Art Unit 1641

12.